REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on May 3, 2005, and the references cited therewith.

Claim 20 is amended, and claims 20 and 23 through 31 are now pending in this application.

A revocation and appointment signed by a representative of the assignee is filed herewith, appointing the undersigned as attorney of record.

§103 Rejection of the Claims

Claims 20 and 23-31 were rejected under 35 USC § 103(a) as being unpatentable over Rhodes (U.S. 5,102,990) in view of Grogg et al. (U.S. 4,510,125). This ground of rejection is respectfully traversed. Applicants note that claim 1 is now amended, and recites that in the kit the second container is one "consisting essentially of" the stabilizer. Applicant understands "consisting essentially of" to include ingredients that do not materially affect the basic character of the stabilizer (e.g., the stabilizer may be in solution and thus the second container also may include water (Claim 26), a physiologically acceptable carrier or diluent (Claim 28) a preservative such as sodium hydrosulfite, or reagents for pH adjustment such as sodium bicarbonate). Applicants further understand the second container to include the vessel itself, such as a vial and stopper, an ampyl, or the like. Finally, Applicants understand the transitional phrase "consisting essentially of" to exclude the second container including either the anti-SSEA-1 IgM monoclonal antibody to be radiolabeled or stannous ion.

As the Office Action notes (see page 3) Rhodes discloses a protein substrate that is to be radiolabeled "mixed with a stannous chloride solution that may ... **include another component such as gentisic acid.**" (Emphasis added.) It is critical that Rhodes only discloses that the protein substrate and the stannous chloride is mixed with the other "component." The Office Action relies upon Example III of Rhodes, columns 15-16, and asserts that in Example III a "pertechnetated solution" is prepared which includes gentisic acid. It is respectfully suggested that this reading is erroneous, particularly in light of claim 1 as amended. Rhodes discloses first that an "Sn (II) reducing solution" was prepared (col. 15, line 40), and that for "each ml of purified protein solution was added 0.66 ml of Sn (II) reducing solution." (col. 15, lines 44-46) As described in Example II, this reduces the protein, which protein was then purified using a

"PD-10 column." The resulting purified material thus contains only Sn (II) complexed and reduced protein which was placed in a sealed vial and frozen. (col. 15, lines 49-51) In a separate operation, as described in the following paragraph (col. 15, lines 53-63), a "pertechnetate reducing solution" is made, which contains "50 mg of gentisic acid, 0.375 μg $SnCl_2$ and 975 μg of sodium potassium tartrate." In the same vial as that containing one protein, the pertechnetate reducing solution is "layered over the frozen, reduced and Sn (II) complexed protein solution and this solution frozen." (col. 15, lines 60-61). Thus there is present, in a single vial, stannous reduced protein (which results in what is called "Sn (II) complexed protein") with a separate frozen layer containing stannous chloride and gentisic acid. It is to this complex of different components that sodium pertechnetate Tc-99m is then added. (Paragraph bridging cols. 15 and 16.). What is of substantive importance is that the gentisic acid (referred to as a "stabilizer" in the Office Action) is present in the same vial with the reduced protein and the stannous agent at the time the radiometal is added. There is no possibility of the gentisic acid being in a "second vial."

The importance of this distinction is apparent from the specification in this application. As the title and entire specification indicates, this application is involved with "post-labeling stabilization" of radiolabeled protein, specifically anti-SSEA-1. This is because, as is stated in the specification, the Applicants "have found that, unexpectedly, when added subsequent to radiolabeling (and subsequent to any incubation period), ascorbic acid and its derivatives result in a radiolabeled substance of superior stability and body." Specification at page 7, line 30 through page 8, line 3. Rhodes teaches only a method in which gentistic acid is present in the vial with the anti-SSEA-1 monoclonal antibody prior to, and during, the radiolabeling step. The inventive step in this application was that superior results could be obtained by adding ascorbic acid after radiolabeling and incubation, rather than having a substance such as gentisic acid present in the composition that is radiolabeled. Thus this application teaches a kit with two separate and distinct vials -- one containing the protein and radiolabeling reagents, principally stannous, and the other vial containing ascorbic acid. Properly understood, it may be seen that Rhodes teaches away from the invention, because Rhodes discloses only combining gentisic acid with stannous and protein to be radiolabeled, while the invention teaches adding the ascorbic acid in a separate and distinct step, after radiolabeling and incubation.

In this context, it is noted that the Office Action suggests that Rhodes teaches that "a pertechnetate reducing solution is generated that contains gentisic acid..." (See Office Action at page 5.) However, the "pertechnetate reducing solution" necessarily contains a stannous solution (in Rhodes stannous is employed in two different processes -- first to reduce disulfide bonds in the protein, and second to reduce pertechnetate). Claim 1 as amended excludes stannous from the second container consisting essentially of the stabilizer.

Thus understood, the invention as now claimed is not obvious over Rhodes in view of Grogg et al. Grogg et al. does not teach components such as the anti-SSEA-1 antibody, and indeed Grogg et al. is concerned primarily with non-proteinaceous compounds, such as organodiphosphonates. The compositions of Grogg et al. are, e.g., a diphosphonate carrier, a tin metal, a stannous compound and a stabilizer. (Col. 10, lines 15-20.) Grogg et al. discloses no more than Rhodes -- for example, Grogg et al. specifically states the lyophilized kit compositions are formed by "co-dissolving the optional carrier and stannous compounds and the stabilizer in an aqueous solution, and freeze-drying the composition..." (Col. 10, lines 60-63). See also col. 11, lines 32-41 (the "stabilizer" is in an aqueous solution that is contacted with tin prior to lyophilization), col. 12, lines 41-55 (a kit with both gentisate stabilizer and a diphosphonate carrier, and thus not meeting the "consisting essentially of" limitation, since the diphosphonate is the material to be radiolabeled), and the paragraph bridging col. 12 and 13 (disclosing various formulations, but all include tin, tin metal, or other forms of stannous).

Conclusion

Applicant respectfully submits that the claims as amended are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (609-495-9197) to facilitate prosecution of this application if any issues remain.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 2 day of ~~October~~ November, 2005

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